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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
09/14/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/553,833	FRERE ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11,15 and 17-25* is/are pending in the application.

4a) Of the above claim(s) *24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11,15 and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refer to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference).

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 16, 2010 has been entered.

Election/Restrictions

To summarize the current election, applicant elected invention group III without traverse. The product claims in their current form are all drawn to the embodiment defined by group III, thus the restriction among groups I-III is hereby withdrawn. Therefore claims 2-5, 7-11, 15, and 19-23 are rejoined.

Claims 24-25 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 5 recites "esters, stearates, glycerides"; however these broad classes of compounds were not initially disclosed as a part of the invention according to the specification. The specification discusses fatty acid esters, fatty acid stearates, and fatty acid glycerides, but not the broad classes of esters, stearates, and glycerides.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-11, 15, and 17-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "said vector an essentially lipophilic nature" which is not a coherent phrase and appears to be missing one or multiple words. This claim also recites "said week bonds capable of detaching said chemical species from said matrix"; however, "bonds" do not detach elements from one another. While the breakage of bonds can detach elements from one another, the bonds themselves are not responsible for the detachment, as the claim currently recites.

Claim 2 recites the term "bioassimilable" however the meaning of this term is not provided and it is unclear what limitation is intended by its recitation.

The claims not explicitly discussed require the limitations of an indefinite claim and do not provide clarity, therefore they are also indefinite.

The following is a quotation of the fourth paragraph of 35 U.S.C. 112:

> Subject to the [fifth paragraph], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Claim 8 are rejected under 35 USC 112, fourth paragraph, for failing to specify a further limitation of the subject matter in the claims they reference.

The limitations of claim 8 are broader than its parent; therefore instead of narrowing the claim it yields a broader breadth.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-11, 17-18, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar (previously cited) in view of Keller (previously cited) and Baker et al. (previously cited).

Kumar teaches particles for oral delivery (see page 234 column 2 paragraph 1).In one embodiment, lipid coated gel chitosan microspheres are taught (see page 247 column 1 paragraph 2 and figure 10; instant claims 4 and 9-10). These microspheres also meet the limitation of the instantly recited "capsule" (see instant claim 11). Specifically, chitosan and the pharmacologically active substance 5-fluorouricil are taught present in the core of a particle that is then coated with the lipid dipalmitoyl phosphalidyl choline (DPPC) (see page 247 column 2 lines 1-14). DPPC is a fatty acid

derivative since it is derived from two palmitic acid groups (see instant claim 1). The dried, lipid coated particles are taught to have a diameters of 250 nm to 300 nm (page 247 column 2 17-19; instant claims 1 and 8). Employing applicants' descriptive language, the chitosan gel microspheres are the essentially hydrophilic matrix and the DPPC is the chemical species that gives the vector an essentially lipophilic nature. Although not explicitly taught by Kumar, it is the position of the Examiner that the interaction between the chitosan core and the DPPC coating would meet the claim limitation of "weak bonds". As figure 9 of Kumar demonstrates, chitosan is a positively charged molecule. The phosphate groups of the DPPC are negatively charged, thus electrostatic interaction would likely occur between these molecules and those of the chitosan (see instant claim 7). Further, hydrogen bonds are also possible between the carbonyl groups of the DPPC and the amines in the chitosan structure, which would also qualify as "weak bonds" (see instant claim 7). Kumar et al. also does not explicitly teach the inclusion of these particles in a gastric protection with a lipophilic compound.

Keller teaches a drug containing particulate vector that is lipophilic and included with a liquid carrier (propylene glycol) in a soft gelatin capsule, where the capsule is coated with an enteric polymeric coating (see column 4 lines 22-29 and example 1; instant claims 1, 18, and 22-23). Such coatings are well known to withstand the acidic environment of the stomach, thereby protecting its cargo and facilitating its delivery in the intestine. Further Keller teaches that the gelatin capsules are negatively affected by the presence of water in the material they contain (see column 4 lines 5-6). Keller does not teach that this liquid carrier is lipophilic.

Baker et al. teach a drug containing lipophilic particulate composition that is taught to be delivered with a pharmaceutically acceptable carrier (see column 25 lines 14-27 and column 26 lines 3-4). Baker et al. go on to teach a set of glycols and oils that are particularly envisioned as such a carrier, where a variety of animal oils, mineral oils, and organic oils are named (see column 26 lines 6-10; instant claims 1 and 17).

The teachings of Keller et al. provide an enteric coated soft gelatin capsule that holds a liquid carrier (polyethylene glycol) and active containing particulates. Baker teaches equivalent liquid carriers for pharmaceutical particulates that include both glycols and oils. It would have been obvious to one of ordinary skill in the art at the time of the invention to combine these teachings and use one of the oils taught by Baker et al. instead of the glycol used as the liquid carrier in the gelatin capsule of Keller et al. It also would have been obvious to employ this gelatin capsule configuration of Baker et al. and Keller et al. in the invention of Kumar as an oral carrier for his particles since they are known for oral delivery. Further, gelatin capsules were well known in the art as oral carriers at the time of the invention and therefore were an option well within the technical grasp of one of ordinary skill in the art at the time of the invention. Again employing applicants' terminology, the oil is the lipophilic component, the gelatin capsule is the gastric protection which is also gastric resistant due to its enteric coating, and the combination of coated microspheres, oils, and coated gelatin capsule are the vector (see instant claims 1 and 22-23). This oral dosage form vector is capable of meets the limitations of instant claim 2. Based upon applicant's disclosure of the same components and configuration as a part of the invention (see instant specification

paragraphs 35, 38-40, 43, 49, 53, and 57) and absent evidence to the contrary, it is the position of the Examiner that the composition of Kumar in view of Keller and Baker et al. would also have the same properties (allows said pharmacologically active substance to pass from the intestinal lumen to the blood, optionally via the interstitial fluid, without denaturation or degradation of said at least one pharmacologically active substance, and upon contact with microvilli present in the intestine during passage through the intestinal lumen, said chemical species detach from said matrix such that said matrix becomes an essentially hydrophilic nature – see instant claims 1 and 3). Therefore claims 1-4, 7-11, 17-18, and 22-23 are obvious over Kumar in view of Keller and Baker et al.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar in view of Keller and Baker et al. as applied to claims 1-4, 7-11, 17-18, and 22-23 above, and further in view of Gao et al. (US PGPub No. 2002/0156124).

Kumar in view of Keller and Baker et al. render obvious the vector of instant claim 1 in the form of an oral dosage form where the gastric protection is a gelatin soft capsule. This modified reference does not explicitly teach that the gastric protection includes alginate.

Gao et al. teach oral dosage forms that include soft capsules which encapsulate a pharmaceutical component (see paragraph 81). The go on to teach that the wall materials of these structures can be cellulose polymers, gelatin, and sodium alginate (see paragraph 82).

As functionally equivalent materials that are each suitable for inclusion in the wall of soft capsules employed as encapsulating materials for oral pharmaceutical compounds to be delivered orally, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize sodium alginate instead of gelatin in the soft capsules of Kumar in view of Keller and Baker et al. This modification would have been obvious as the simple substitution of one known element for another to achieve a predictable outcome. Therefore claim 15 is obvious over Kumar in view of Keller, Baker et al., and Gao et al.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar in view of Keller and Baker et al. as applied to claims 1-4, 7-11, 17-18, and 22-23 above, and further in view of McCullough et al. (US Patent No. 6,114,356).

Kumar in view of Keller and Baker et al. render obvious the vector of instant claim 1 in the form of an oral dosage form where the liquid vehicle in the gelatin soft capsule is an organic oil, mineral oil, or animal oil. This modified reference does not explicitly teach that glycerides or lipophilic polymers are also present.

McCullough et al. teach soft gelatin capsules employed as oral dosage forms (see column 11 lines 16-18). They go on to teach conventional liquid vehicles that are known in the art for such capsules and these include mineral oil, triglycerides, polysorbates, and their combinations (see column 11 lines 22-36). Polysorbates are surfactants that have a lipophilic side chain therefore they meet the limitations of lipophilic polymer (see instant claim 5).

It would have been obvious to one of ordinary skill in the art at the time of the invention to select a combination of oil as recited by Kumar in view of Keller and Baker et al. with polysorbate or triglycerides as the liquid vehicle in the soft gelatin capsule because McCullough et al. teach that such combinations were conventional in the art. This modification would have been obvious as the simple substitution of one known element for another to achieve a predictable outcome. Therefore claim 5 is obvious over Kumar in view of Keller and Baker et al., and McCullough et al.

Claims 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar in view of Keller and Baker et al. as applied to claims 1-4, 7-11, 17-18, and 22-23 above, and further in view of Ma et al. (Journal of Pharmaceutical Sciences 2002 91:1396-1404).

Kumar in view of Keller and Baker et al. render obvious the vector of instant claim where the matrix is a lipid coated chitosan gel microsphere intended for oral delivery of the contained pharmacologically active agent. This modified reference does not explicitly teach that the pharmacologically active agent is insulin.

Ma et al. teach chitosan nanoparticles as oral carriers for insulin (see page 1396 column 1-page 1397 column 1 line 3). Insulin is a protein capable of being denatured or degraded upon direct oral administration (see instant claims 19-21). These particles are sized in the same range as those taught for the microspheres of Kumar in view of Keller and Baker et al. (see figure 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ insulin as the drug cargo in the chitosan microspheres of Kumar in view of Keller and Baker et al. based upon the teachings by Ma et al. that this protein was known at the time of the invention to be orally delivered from chitosan nanoparticles of the same size. This modification would have been obvious as the simple substitution of one known element for another to achieve a predictable outcome. Therefore claims 19-21 are obvious over Kumar in view of Keller, Baker et al., and Ma et al.

Response to Arguments

Applicants' arguments, filed December 16, 2010, have been fully considered but they are not persuasive.

Regarding rejection under 35 USC 103(a):

Applicants argue that the rejection based upon Kumar et al. in view of Keller and Baker et al. was predicated on an "obvious to try" rationale for achieving the claimed property of detachment of the outer lipophilic coating due to the action of intestinal microvilli and that the combination of references do not render obvious the selection of a fatty acid derivative as the lipophilic chemical species in the coating. This was not the basis of the rejection therefore this argument is not pertinent to the rejection of record. In addition, Kumar et al. explicitly exemplify a hydrophilic chitosan gel matrix core that is modified by a coating of the fatty acid derivative DPPC. A *prima facie* case of obviousness has been established based upon the components and component

configurations that are claimed. The burden shifts to the applicant to come forward with arguments and/or evidence to rebut the *prima facie* case.

Applicants also argue that Kumar et al do not teach detachment of the DPPC layer. Applicants exemplify the vector invention as a core with a combination of compounds carrying positive and negative charge and a coating carrying a negative charge. Kumar et al. teach a core with a compound carrying a positive charge and a coating carrying a negative charge. In both instances electrostatic interactions would be expected to occur between the core and coating components. Applicants teach electrostatic bonds as "weak" bonds capable of being detached due to contact with microvilli upon passage through the intestinal wall (see instant specification paragraphs 39 and 42). Therefore, if the coating of applicants' exemplified vector has a coating capable of being detached due to contact with microvilli upon passage through the intestinal wall, then so does that of Kumar et al. since it has the same claimed components and weak bonds. Applicants provide no evidence that that the particles of Kumar et al. do not have this property, therefore the claims are still deemed obvious over Kumar et al. in view of Keller and Baker et al.

Applicants argue that there was no expectation of success for the selection of a fatty acid, but the claims are not limited to fatty acids as the chemical species. Given that fatty acid derivatives are also recited option in the instant claims and the evidence currently of record, the exemplified composition of Kumar et al. meets the limitations of the matrix and chemical species with their associated properties.

Applicants discuss an unexpected result having been achieved by the selection of fatty acid derivatives for the chemical species, but provide no evidence to support these statements. The arguments of counsel cannot take the place of evidence in the record.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

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Primary Examiner, Art Unit 1634